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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/750,101	05/01/97	DOLLY	J ALRGN.054CP1

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CARLOS O. FISHER
LEGAL DEPARTMENT, T2-2E
ALLERGAN, INC.
P. O. BOX 19534, 2525 DUPONT DRIVE.
IRVINE CA 92623-9534

EXAMINER

MINNIFIELD, N

ART UNIT

PAPER NUMBER

1645

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DATE MAILED:

07/07/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
08/750,101

Applicant(s)

DOLLY ET AL

Examiner
N. M. Minnifield

Group Art Unit
1645



☒ Responsive to communication(s) filed on Mar 19, 1999

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 33-46 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 33-46 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

1. The request filed on March 19, 1999 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/750101 is acceptable and a CPA has been established. An action on the CPA follows.
2. Applicants' amendment filed March 19, 1999 is acknowledged and has been entered. Claims 1-4, 7, 8 and 22-25 have been canceled. New claims 33-46 have been added. Claims 33-46 are now pending in the present application.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
4. Claims 33-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 33-35 and 37-41 are

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vague and indefinite in the recitation of the specific amino acid modifications as set forth in claim 35. It is not clear if these mutations are in the heavy chain or light chain. What is a botulinum toxin other than botulinum toxin A with a modification at the site corresponding to the histidine at amino acids position 227 for example? Claims 39 and 44 are indefinite because they contain the abbreviations SNAP-25 and VAMP. Full terminology should be in each instance in the claims without the additional use of redundant abbreviations in parentheses or otherwise. Correction is required.

5. Claims 33, 34, 36-38, 40, 42, 43 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bizzini taken with Fraenkel-Conrat et al.

Bizzini teaches a composition that comprises tetanus toxin and is bound to a thiol group, and that this composition can be used to transport agents for medicine to the central nervous system (abstract; col. 2, l. 56-60). Bizzini teaches the use of fragments of the tetanus toxin that are atoxic (i.e. inactive) (col. 2, l. 36-45). Bizzini teaches that medicines can be transported into the nervous system via the

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medicine being bound to the thiolated polypeptide compound (tetanus toxin), employed as a transport agent (col. 6, l. 1-40; claims). Bizzini et al teaches the concept of inactivating the neurotoxins. The prior art teaches the claimed invention except or the concept of amino acid modification of the neurotoxin. However, Fraenkel-Conrat et al teach amino acid substitution of the light chain of tetanus toxin. Fraenkel-Conrat et al also teach fusion (attachment) of another bioactive molecule. Fraenkel-Conrat et al teach that the mutant light chain of tetanus toxin was inactive. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the inactive and modified neurotoxin of Fraenkel-Conrat et al in a composition for the purpose of treating tetanus infection. Both references teach the concept of using inactive neurotoxins. The claimed invention is prima facie obvious in view of Bizzini taken with Fraenkel-Conrat et al, absent any convincing evidence to the contrary.

The rejection is maintained for the reasons of record. Applicant's arguments filed July 30, 1998 have been fully considered but they are not

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persuasive. Applicants have asserted that the light chain is attenuated to make the molecule non-toxic and that thiolation of the toxin is not disclosed or claimed. Applicants have asserted that the prior art toxins do not have the same properties as the claimed invention (intraneuronal retrograde transport). Applicants have asserted that there is no suggest to combine the prior art references. It is noted that this is a combination 103 obviousness rejection over what Bizzini et al in view of Fraenkel-Conrat taken together would suggest to person having ordinary skill in the art at the time the invention was made. Bizzini suggests reducing the toxicity of the tetanus toxin therefore it would have been obvious to a person having ordinary skill in the art at the time the invention was made to modify the neurotoxin by any means (inactivation, attenuation, deletion or substitution of amino acids) which would alter the neurotoxin. The claimed invention is prima facie obvious in view of the prior art absent any convincing evidence to the contrary.

With regard to Applicants' March 19, 1999 amendment, the claims are directed to a modified toxin that has inactivated light chain (via mutation) and

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inactivated heavy chain, and a drug or other bioactive molecule. The prior art teaches modification of the light chain by amino acid modification and reconstitution of the heavy chain with the light chain after both have been inactivated and that this provides a mutant that is not lethal. Bizzini suggests reducing the toxicity of the tetanus toxin therefore it would have been obvious to a person having ordinary skill in the art at the time the invention was made to modify the neurotoxin by any means (inactivation, attenuation, deletion or substitution of amino acids) which would alter the neurotoxin and Fraenkel-Conrat et al teaches how to obtain such mutations. The claimed invention is prima facie obvious in view of the prior art absent any convincing evidence to the contrary.

6. No claims are allowed.
7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

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8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is (703) 305-3394. The examiner can normally be reached on Monday-Thursday from 7:00 AM-4:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D., can be reached on (703) 308-3995. The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

N. M. Minnifield

July 6, 1999


NITA MINNIFIELD
PRIMARY EXAMINER